Background Notes for Discussion with Oxitec, June 9, 2017

OPP Interactions with Oxitec:

Meeting between EPA, FDA, and Oxitec, February 9, 2017

- Given FDA's January 2017 proposal ("Guidance 236") to transfer oversight of GE mosquitoes to EPA, participants discuss what regulatory pathways and options are available to Oxitec, and what level of review would be needed.
- Since EPA does not have data requirements for this type of product, we would work with Oxitec to define reasonable data to support registration; estimating a 1-year review time.
- Assuming data Oxitec had provided to FDA to support their proposed Investigational New Animal Drug (INAD) trial would be sufficient to support an Experimental Use Permit (EUP), EPA indicated that the review could be much shorter than the typical 7-month review time under PRIA.
- OPP said Section 18 Emergency Exemptions are typically approved in about 50 days, though for a novel product is could be slightly longer.

Teleconference between OPP, OGC, and Oxitec, February 17, 2017

- EPA has determined that Oxitec can immediately proceed with an experimental use permit application involving their GE mosquitoes and that EPA could issue the EUP before 236 is finalized.
- EPA has determined a Section 18 involving Oxitec's GE mosquitoes can immediately be submitted and EPA can begin review, but 236 would have to be final before EPA grants the Section 18.
- EPA and FDA are ready to have a joint meeting with Oxitec as soon as the firm is available to discuss additional details and EPA-FDA intersects.

Meeting between EPA, FDA, and Oxitec, March 7, 2017

- EPA provided specific guidance to Oxitec on how to submit an application for an EUP, data EPA expects to need including information on the novel proteins produced, and that rationales supported with data could be used to support an EUP.
- EPA also provided further guidance on the Sec 18 and Sec 3 pathways and affirmed timeframes of about 50 days and 13 months respectively.

Teleconference between EPA and Oxitec, April 13, 2017

- EPA regulatory and technical staff discussed details of data needs with Oxitec's technical and regulatory staff.

EPA and Florida Department of Agriculture (FDACS) staff visit to Oxitec Florida Facility, May 2, 2017

- EPA and FDACS staff observe Oxitec's Florida mosquito-rearing facility and discuss technical and regulatory issues and options as well as likely timeframes with Oxitec technical staff and Florida Keys Mosquito Control District staff.

Interagency meeting hosted by HHS at request of Oxitec, May 17, 2017 (meeting summary attached)

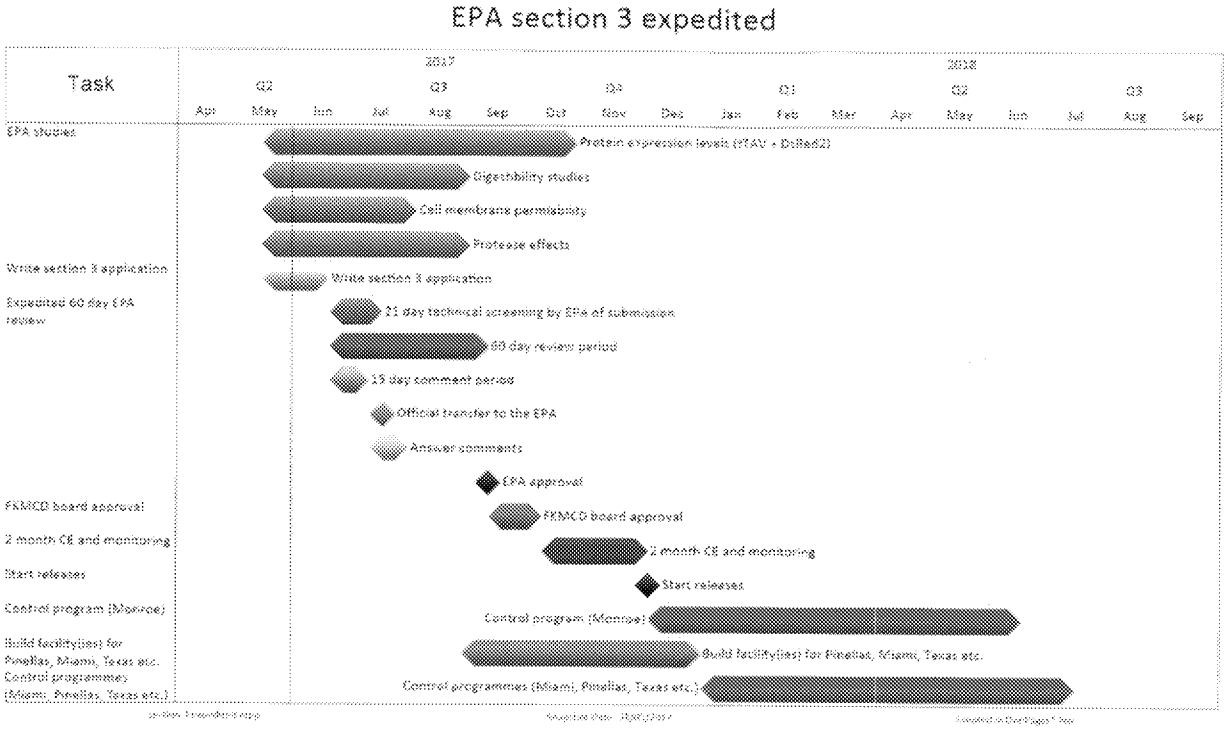
- EPA and FDA provided further guidance to Oxitec on regulatory pathways that would allow Oxitec to begin field testing mosquitoes as soon as possible.

- EPA reaffirmed that we can review and issue an EUP before FDA transfers jurisdiction to EPA, and that EPA could review, but not issue a Sec 18, before we have jurisdiction.
- EPA agreed to continue dialog with Oxitec on specific data needs to support an EUP and Sec 18 versus a full Sec 3, and to expedite reviews and decision-making given the potential public health benefits.
- Timelines for EPA decisions, assuming Oxitec's submissions are complete, included
    - EUP – seven months or less per PRIA – jurisdiction not required
    - Section 18 – about 2 months, not a PRIA action – EPA must have jurisdiction to issue
    - Section 3 – 13 months or less per PRIA, EPA must have jurisdiction to begin review (see timeline from Oxitec at bottom)
- Oxitec indicated that they preferred to continue to pursue an INAD with FDA while also pursuing available EPA pathways.
- Oxitec suggested that a viable path would be testing under FDA INAD oversight during the Summer/Fall of 2017 with an EPA EUP submission sometime in the Fall of 2017 and EUP issuance (and transfer of jurisdiction) occurring in February 2018 for field trials in the Spring/Summer 2018.

Teleconference between OPP and Oxitec technical staff, May 18, 2017

- Oxitec describes specific elements of the data they are generating and timeframes for expected completion.

Keith Matthews provides to EPA a Sec 3 timeline dated May 31, 2017, showing a 3-month review time



BPPD considerations on Matthews's June 2017 schedule/timeframe:

- This pre-supposes there is an emergency that warrants such a schedule that could not otherwise be addressed via Section 18 or 5. To rush a Sec 3 decision could undercut the significant public benefits see this technology may offer.

- This timeframe is aligned with a Section 18 action where less data are needed and an emergency exists.

- While this is a promising technology and the Agency is pleased that authority to regulate these types of products is being transferred to EPA this is a novel technology based on genetic engineering that is very likely to elicit vigorous public interest on all sides of the issue.

- Completing a new active ingredient registration within 90 days of receipt would be unprecedented in OPP.

- We have not formally reviewed the studies that were part of the EA, nor the overseas efficacy data to supplement expected U.S. efficacy data generated under an EUP.

- With respect to the efficacy data, to grant a Section 3 w/o US efficacy testing runs counter to long established RD policy.

- The ESA approach underlying the original EA was about to be challenged legally and that FDA had identified deficiencies in Oxitec's new submission.

- A Section 3 with no geographical restrictions greatly complicates the ESA assessment. Making a quick, broad determination seems to be a monumental task and likely open to legal vulnerability.

- The company has started doing 4 studies we identified as being needed for a Section 3. We would have to condition a registration on some or all of those studies leaving potential gaps in the assessment. The primary use of the data was to avoid the need for numerous non-target organism studies in support of a broad-based ESA finding.

- The timeline envisions only a single 15-day comment period at the Notice of Receipt stage. The Notice of Receipt (NOR) simply informs the public that the action has been initiated and the Agency review is ready to begin. While we may receive substantive commentary during that time, stakeholders often provide significant comment on assessments, data, and proposed decisions.

- This timeline has no opportunity for independent scientific peer review. We believe building that step in will build support for this technology, as well as building trust in EPA's objective peer review process.

- Attempting to meet this time frame would create precedent and pressure for "level-playing-field" treatment by a wide range of stakeholders.

Oxitec's May 17 Timeline for Section 3: